

IN THE CLAIMS

1. (Original) A method for inactivating a nuclear localization signal of a protein comprising contacting the protein with a compound that is capable of stable reversible binding with basic amino acid residues of the nuclear localization signal of the protein.

2. (Original) A method for inhibiting importation of a protein into the nucleus of a cell comprising contacting the protein with a compound that is capable of stable reversible binding with basic amino acid residues of the nuclear localization signal of the protein.

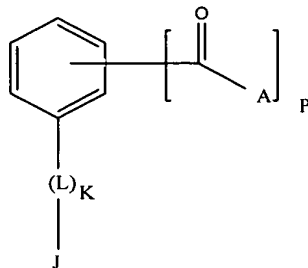
3. (Original) A method for targeted inactivation of a nuclear localization signal of a protein in a complex comprising contacting the protein with a compound that is capable of:

- (a) interacting with a molecule in a complex having a specific docking site which is positioned proximately to a nuclear localization signal of a protein in the complex; and
- (b) forming stable reversible covalent interactions with basic amino acid residues of the nuclear localization signal of the protein.

4. (Original) The method of Claim 3, wherein the compound forms Schiff bases with lysine residues of the nuclear localization signal of the protein.

5. (Original) The method of Claim 3, wherein the compound forms stable reversible covalent interactions with arginine residues of the nuclear localization signal of the protein.

6. (Currently Amended) A method for targeted inactivation of a nuclear localization signal of a protein comprising contacting the protein with a compound according to the formula:



(I)

wherein A, independently, = CH₃, CH₂CH₃, COH, COCH₃, COCH₂CH₃, CH₂COCH₃, CH₂COCH₂CH₃, C(CH₃)₂COCH₃, or C(CH₃)₂COCH₂CH₃; P = 1 or 2; L is a linker group containing an S, O, N or C atom; K = 0 or 1; and wherein J represents (i) a saturated or unsaturated, substituted or unsubstituted, straight or branched acyclic hydrocarbon group; (ii) a saturated or ~~saturated~~ unsaturated, substituted or unsubstituted, straight or branched acyclic group containing hetero atoms such as nitrogen, sulfur or oxygen; (iii) a substituted or unsubstituted, saturated or aromatic, mono- or poly- cyclic group having 3 to 20 carbon atoms; or (iv) a substituted or unsubstituted, saturated or aromatic, mono- or poly- heterocyclic group having 3 to 20 atoms, at least one of which is a nitrogen, sulfur or oxygen.

7. (Canceled)

8. (Canceled)

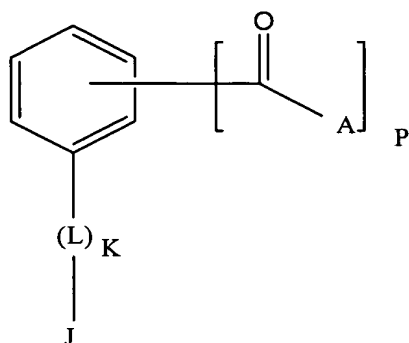
9. (Currently Amended) The method of ~~Claim 3, 4 or 5~~ Claim 3, wherein the docking site is on the protein having the nuclear localization signal.

10. (Currently Amended) The method of ~~Claim 3, 4, 5, 6, 7 or 8~~ Claim 3, wherein the protein is derived from a human immunodeficiency virus, influenza virus, hepatitis virus, herpes simplex virus, papillomavirus, parvovirus or measles virus.

11. (Original) The method of Claim 3, wherein the docking site is on the human immunodeficiency virus reverse transcriptase and the nuclear localization signal is in the human immunodeficiency virus matrix antigen.

12. (Original) A method for identifying compounds that are capable of targeted inactivation of the nuclear localization signal of a protein comprising:

(a) contacting an immobilized cellular receptor moiety with a protein comprising a nuclear localization signal, and a compound having the formula:



wherein A, independently, = CH₃, CH₂CH₃, COH, COCH₃, COCH₂CH₃, CH₂COCH₃, CH₂COCH₂CH₃, C(CH₃)₂COCH₃, or C(CH₃)₂COCH₂CH₃; P = 1 or 2; L is a linker group containing an S, O, N or C atom; K = 0 or 1; and wherein J represents (i) a saturated or unsaturated, substituted or unsubstituted, straight or branched acyclic hydrocarbon group; (ii) a saturated or unsaturated, substituted or unsubstituted, straight or branched acyclic group containing hetero atoms such as nitrogen, sulfur or oxygen; (iii) a substituted or unsubstituted, saturated or aromatic, mono- or poly- cyclic group having 3 to 20 carbon atoms; or (iv) a substituted or unsubstituted, saturated or aromatic, mono- or poly- heterocyclic group having 3 to 20 atoms, at least one of which is a nitrogen, sulfur or oxygen;

(b) measuring the binding of the protein to the immobilized cellular receptor moiety; and

(c) comparing the quantity of the protein bound to the quantity of protein bound in the absence of the compound,

where a reduction in the quantity of the bound protein in the presence of the compound is indicative of targeted inactivation of the nuclear localization signal by the compound.

13. (Original) The method of Claim 12, wherein the protein is in a complex.

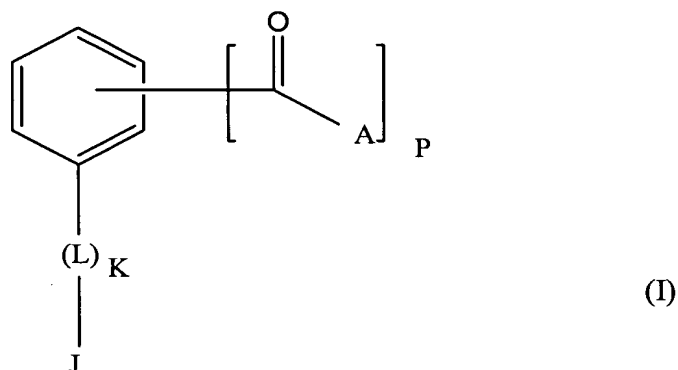
14. (Original) The method of Claim 12, wherein the protein is derived from a human immunodeficiency virus, influenza virus, hepatitis virus, herpes simplex virus, papillomavirus,

parvovirus or measles virus.

15. (Original) The method of Claim 12, wherein the cellular receptor moiety is karyopherin α .

16. (Original) A method for identifying compounds that are capable of targeted inactivation of the nuclear localization signal of a viral nucleoprotein complex comprising:

(a) contacting an immobilized karyopherin α with a viral nucleoprotein complex contained in a cytoplasmic extract, said complex comprising viral nucleic acid and said cytoplasmic extract prepared from cells infected by the virus, and a compound having the formula:



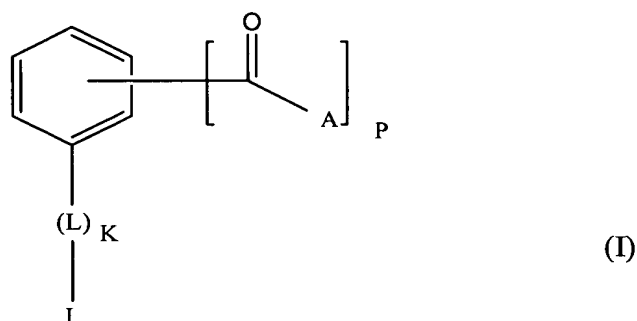
wherein A, independently, = CH₃, CH₂CH₃, COH, COCH₃, COCH₂CH₃, CH₂COCH₃, CH₂COCH₂CH₃, C(CH₃)₂COCH₃, or C(CH₃)₂COCH₂CH₃; P = 1 or 2; L is a linker group containing an S, O, N or C atom; K = 0 or 1; and wherein J represents (i) a saturated or unsaturated, substituted or unsubstituted, straight or branched acyclic hydrocarbon group; (ii) a saturated or unsaturated, substituted or unsubstituted, straight or branched acyclic group containing hetero atoms such as nitrogen, sulfur or oxygen; (iii) a substituted or unsubstituted, saturated or aromatic, mono- or poly- cyclic group having 3 to 20 carbon atoms; or (iv) a substituted or unsubstituted, saturated or aromatic, mono- or poly- heterocyclic group having 3 to 20 atoms, at least one of which is a nitrogen, sulfur or oxygen;

- (b) measuring the binding of said complex to the immobilized karyopherin α by quantitating the amount of viral nucleic acids associated with said complex; and
- (c) comparing the quantity of the nucleic acid bound to the quantity of nucleic acid bound in the absence of the compound;

wherein a reduction in the quantity of the bound nucleic acid in the presence of the compound is indicative of targeted inactivation of the nuclear localization signal by the compound.

17. (Original) A compound that is capable of:

- (a) interacting with a molecule in a complex having a specific docking site which is positioned proximately to a nuclear localization signal of a protein in the complex; and
- (b) forming stable reversible covalent interactions with basic amino acid residues of the nuclear localization signal of the protein; and having the formula:



wherein A, independently, = CH_3 , CH_2CH_3 , COH , COCH_3 , COCH_2CH_3 , CH_2COCH_3 , $\text{CH}_2\text{COCH}_2\text{CH}_3$, $\text{C}(\text{CH}_3)_2\text{COCH}_3$, or $\text{C}(\text{CH}_3)_2\text{COCH}_2\text{CH}_3$; $P = 1$ or 2 ; L is a linker group containing an S, O, N or C atom; $K = 0$ or 1 ; and wherein J represents (i) a saturated or unsaturated, substituted or unsubstituted, straight or branched acyclic hydrocarbon group; (ii) a saturated or unsaturated, substituted or unsubstituted, straight or branched acyclic group containing hetero atoms such as nitrogen, sulfur or oxygen; (iii) a substituted or unsubstituted,

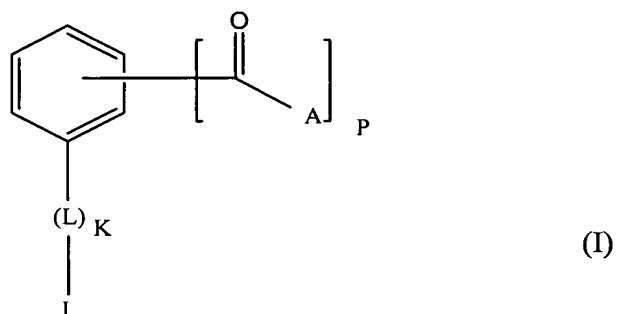
saturated or aromatic, mono- or poly- cyclic group having 3 to 20 carbon atoms; or (iv) a substituted or unsubstituted, saturated or aromatic, mono- or poly- heterocyclic group having 3 to 20 atoms, at least one of which is nitrogen, sulfur or oxygen.

18. (Original) The compound of Claim 17, wherein the protein is derived from a virus.

19. (Original) The compound of Claim 17, wherein the protein is derived from a human immunodeficiency virus, influenza virus, hepatitis virus, herpes simplex virus, papillomavirus, parvovirus or measles virus.

20. (Original) A method of preventing productive infection by a virus of a proliferating population of cells, which comprises preventing importation of a complex containing viral nucleic acid or viral protein into the nucleus of a cell in the population.

21. (Currently Amended) The method of Claim 20, which further comprises the administration of an effective amount of a pharmaceutical composition containing a compound according to the formula:



wherein A, independently, = CH₃, CH₂CH₃, COH, COCH₃, COCH₂CH₃, CH₂COCH₃, CH₂COCH₂CH₃, C(CH₃)₂COCH₃, or C(CH₃)₂COCH₂CH₃; P = 1 or 2; L is a ~~linker~~ linker group containing an S, O, N or C atom; K = 0 or 1; and wherein J represents (i) a saturated or unsaturated, substituted or unsubstituted, straight or branched acyclic hydrocarbon group; (ii) a saturated or unsaturated, substituted or unsubstituted, straight or branched acyclic group

containing hetero atoms such as nitrogen, sulfur or oxygen; (iii) a substituted or unsubstituted, saturated or aromatic, mono- or poly- cyclic group having 3 to 20 carbon atoms; or (iv) a substituted or unsubstituted, saturated or aromatic, mono- or poly- heterocyclic group having 3 to 20 atoms, at least one of which is nitrogen, sulfur or oxygen.

22. (Original) The method of Claim 20, which comprises the administration of an effective amount of a pharmaceutical composition containing Compound No. 2 as an active ingredient.

23. (Original) The method of Claim 1, wherein the compound is capable of forming tandem Schiff bases with lysine residues of the nuclear localization signal of the protein.

24. (Original) The method of Claim 1, wherein the compound is capable of forming stable reversible adducts with arginine residues of the nuclear localization signal of the protein.

25. (Currently Amended) The method of ~~Claim 3, 4, 5, 6, 7 or 8~~ Claim 3, wherein the protein is a transcription factor.

26. (New) The compound of Claim 17, wherein $K = 1$.

27. (New) The compound of Claim 17, wherein $K = 1$ and L is a linker group containing an O atom.

28. (New) The compound of Claim 17, wherein $K = 1$, L is a linker group containing an O atom, and J is (iv) a substituted or unsubstituted, saturated or aromatic, mono- or poly- heterocyclic group having 3 to 20 atoms, at least one of which is nitrogen, sulfur or oxygen.

29. (New) The compound of Claim 17, wherein $K = 1$ and L is -O-.

30. (New) The compound of Claim 17 wherein $K = 1$, L is a linker group containing an O atom, and J is a substituted or unsubstituted five or six membered ring having 1-4 hetero ring atoms, at least one of which is nitrogen and the remainder of which are selected from the group consisting of nitrogen, oxygen, sulfur, and a combination thereof.

31. (New) The compound of Claim 17, wherein K = 1, L is a linker group containing an O atom, and J is selected from the group consisting of pyrimidine, pyridine, pyrrole, imidazole, thiazole, isothiazole, isoxazole, furazan, pyrrolidine, piperidine, imidazolidine, piperazine, oxazole, tetrazole, pyrazole, triazole, oxadiazole, and thiodiazole, and may be unsubstituted or substituted with one or more substituents selected from the group consisting of alkyl, alkoxy, phenoxy, alkenyl, alkynyl, phenylalkyl, hydroxyalkyl, haloalkyl, aryl, arylalkyl, alkyloxy, alkylthio, alkenylthio, phenylalkylthio, hydroxyalkylthio, alkylthiocarbamylthio, phenyl, cyclohexyl, pyridyl, piperidinyl, alkylamino, amino, nitro, mercapto, cyano, hydroxyl, halogen, and a combination thereof.

32. (New) The compound of Claim 17, wherein K = 1, L is -O-, and J is a substituted or unsubstituted pyrimidine group.

33. (New) The method of Claim 6, wherein the protein is derived from a human immunodeficiency virus, influenza virus, hepatitis virus, herpes simplex virus, papillomavirus, parvovirus or measles virus.

34. (New) The method of Claim 6, wherein the protein is a transcription factor.